



NOTES

WATER SOLUBLE VITAMINS DEFICIENCY

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- **Vitamin:** micronutrient that participates in essential cellular function

CAUSES

- Insufficient water-soluble vitamin intake
→ ↑ demand, malabsorption, loss → insufficient for body's metabolic needs

COMPLICATIONS

- Chronic water-soluble vitamin deficiency → specific clinical disorders

SIGNS & SYMPTOMS

- See individual disorders

DIAGNOSIS

OTHER DIAGNOSTICS

- History, clinical presentation

TREATMENT

OTHER INTERVENTIONS

- ↑ dietary intake
- Synthetic formulation supplementation
- Address complications

FOLATE (VITAMIN B₉) DEFICIENCY

[osms.it/folate-\(vitamin-b₉\)-deficiency](https://osms.it/folate-(vitamin-b9)-deficiency)

PATHOLOGY & CAUSES

- Insufficient folate (pteroylglutamic acid) for body's metabolic needs
- Body cannot synthesize, normally maintains low stores
- Folate must be obtained in diet; lack for several weeks → deficiency
- Folate deficiency → impaired DNA synthesis during erythropoiesis (cell cycle S-phase delay) → uncoordinated cytoplasm, nuclei maturation in erythroblasts (nuclear-cytoplasmic asynchrony) → ineffective hematopoiesis

→ ↑ erythroid apoptosis + abnormally large erythrocytes (macrocytosis) → defective cells with fragile membranes → ↓ red blood cell (RBC) lifespan → anemia

Sources of folate

- Present naturally in plant (especially dark **green leafy vegetables**), animal products (especially liver)
- Folic acid available in dietary supplements, fortified foods (e.g. cereals)

Recommended dietary allowances (RDAs)

- Folate RDAs listed as micrograms of dietary folate equivalents (DFEs), reflect

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higher bioavailability in food vs. supplement

- **Child 9–13:** 300mcg DFE
- **14+:** 400mcg DFE
- **Pregnancy:** 600mcg
- **Lactation:** 500mcg

RISK FACTORS

Insufficient diet

- **Alcohol abuse**
 - Impairs folate absorption, metabolism; accelerates breakdown
- Chronic systemic disease; mental illness; advanced age
- Food insecurity
- Self-imposed dietary restrictions (e.g. vegan)
- ↓ vitamin C (cofactor for folate metabolism)

Adequate diet but increased requirements

- **Pregnancy**, lactation, malignancy
- Disease state with ↑ cellular turnover (e.g. chronic hemolysis, exfoliative skin disease)

Malabsorption

- E.g. celiac disease, inflammatory bowel disease, gastric surgery, achlorhydria

Metabolic interference from medication

- E.g. methotrexate (folate antagonist), phenytoin, trimethoprim

Hereditary forms

- Hereditary folate malabsorption (HFM)
 - Loss-of-function mutation of PFCT gene encoding for proton-coupled folate transporter (rare, autosomal recessive disorder)
- Infantile cerebral folate deficiency
 - Autoantibody against folate receptor in choroid plexus → prevents folate transport across blood-brain barrier

COMPLICATIONS

- **Megaloblastic anemia**
- Insufficient folate during gestation → ↑ **neural tube defect risk**
- Developmental delay, neurological disorders (child)

SIGNS & SYMPTOMS

- Megaloblastic anemia
 - Hypoxemia, tissue hypoxia → fatigue, activity intolerance, pallor, ↑ heart rate
- ↑ hemolysis → jaundice
- Atrophic **glossitis**, angular stomatitis, anorexia, nausea, diarrhea
- Hereditary folate malabsorption
 - Manifests at age 1–3 months
 - Failure to thrive, neurologic deterioration, megaloblastic anemia
- Infantile cerebral folate deficiency
 - Manifests at age 4–6 months
 - Irritability, ↓ sensorineural hearing, seizure, developmental delay, sleep disturbance → visual disturbance/loss

DIAGNOSIS

LAB RESULTS

- ↓ RBC count; ↓ reticulocyte count; evidence of megaloblastic anemia (↑ mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH))
- **Macrocytosis**, anisocytosis, poikilocytosis, **hypersegmented** neutrophils
- ↑ hemolysis markers
 - ↓ indirect bilirubin, ↓ lactate dehydrogenase, ↓ haptoglobin
- ↓ serum folate
- Hypercellular bone marrow
- Infantile cerebral folate deficiency
 - Cerebrospinal fluid (CSF) assay shows ↓ 5-methyltetrahydrofolate
 - Serum, RBC folate normal

TREATMENT

OTHER INTERVENTIONS

- Address complications (e.g. neurologic manifestation)
- ↑ dietary folate intake
- **Folic acid supplementation** (synthetic formulation)

NIACIN (VITAMIN B3) DEFICIENCY

[osms.it/niacin-\(vitamin-b3\)-deficiency](https://osms.it/niacin-(vitamin-b3)-deficiency)

PATHOLOGY & CAUSES

- Insufficient niacin (nicotinic acid, nicotinamide) for body's metabolic needs
 - Niacin obtained in diet
 - Liver converts **tryptophan to niacin** (60g tryptophan = 1mg niacin)
- Active forms
 - Nicotinamide adenine dinucleotide (**NAD⁺**), nicotinamide adenine dinucleotide phosphate (**NADP⁺**)
- Moderate/↑ doses of niacin supplement → ↓ **total/low-density lipoprotein** (LDL) cholesterol

Sources of niacin

- Present in plant, animal products (e.g. dairy products, meat, grain (↓ corn), legumes, seeds)
- Dietary supplement; enriched grain, cereal, milk

RDAs

- Children 9–13: 12mg
- 19+ male: 16mg; 19+ female: 14mg
- Pregnancy: 18mg
- Lactation: 14mg

RISK FACTORS

Insufficient niacin/tryptophan intake

- Alcohol abuse
- Self-imposed dietary restrictions
- Chronic systemic disease; mental illness; advanced age
- Food insecurity
- Corn-based diet (unless corn treated with alkali, e.g. tortillas)

Malabsorption

- E.g. bariatric surgery, malabsorptive disease states
- **Hartnup disorder: defective tryptophan absorption**

Metabolic defects

- E.g. carcinoid syndrome → impaired tryptophan metabolism

Accelerated niacin depletion

- Prolonged isoniazid use → ↓ pyridoxal phosphate (active form of vitamin B6) → ↑ tryptophan synthesis

Tryptophan-to-niacin conversion inhibited by medication

- E.g. phenobarbital, chloramphenicol, pyrazinamide

COMPLICATIONS

- Pellagra



Figure 53.1 A desquamating rash on the skin of an individual who presented with diarrhea and confusion. The diagnosis was confirmed as pellagra.

SIGNS & SYMPTOMS

- **Dermatitis**
 - Photosensitive, pigmented
- **Diarrhea**
 - Potentially also vomiting
- **Dementia**
 - Potentially also anxiety, disorientation
- **Death**
 - Untreated pellagra potentially fatal

DIAGNOSIS

LAB RESULTS

- ↓ N-methylnicotinamide (niacin metabolism product)

TREATMENT

OTHER INTERVENTIONS

- Niacin supplementation
- ↑ dietary niacin/tryptophan
- Address complications

VITAMIN B12 DEFICIENCY

osms.it/vitamin-b12-deficiency

PATHOLOGY & CAUSES

- Insufficient B₁₂ for body's metabolic needs
- Active **cobalamin** (coenzyme)
forms: methylcobalamin, 5-deoxyadenosylcobalamin
- Dietary cobalamin in food protein → gastric hydrochloric acid, protease-free cobalamin → cobalamin + intrinsic factor complex → distal ileum absorption
- Cobalamin essential for metabolic reactions involving hematopoiesis; protein, DNA, RNA, myelin **synthesis**; gastrointestinal tract mucosa maintenance
 - **Methylcobalamin**: **methionine synthase** (folate-dependent enzyme) **cofactor** → methionine synthase catalyzes homocysteine remethylation to form methionine (essential amino acid for tissue growth/repair; hormone, protein, purine, pyrimidine synthesis)
 - **5-deoxyadenosylcobalamin**: **L-methylmalonyl-coenzyme A conversion** to succinyl CoA → enters citric acid cycle → lipid, protein energy production
- Impaired DNA synthesis during erythropoiesis (e.g. cell cycle S-phase delay) → uncoordinated cytoplasm,

nuclei maturation in erythroblasts (nuclear-cytoplasmic asynchrony) → ineffective hematopoiesis → ↑ erythroid apoptosis, abnormally large erythrocytes (macrocytosis) → defective cells with fragile membranes → ↓ RBC lifespan → anemia

Sources of cobalamin

- **Animal products** (meat, egg, dairy)
- Supplements, enriched food

RDAs

- **Child 9–13**: 1.8mcg
- **14+**: 2.4mcg

RISK FACTORS

Insufficient intrinsic factor

- **Pernicious anemia**
 - Autoimmune condition destroys parietal cells → ↓ intrinsic factor production → cobalamin not absorbed
- Gastrectomy, bariatric surgery
- Gastric atrophy

Malabsorption

- Achlorhydria (acid promotes gastric mucosa absorption)
 - ↑ age → ↑ risk
 - ↓ acid due to medication (e.g. antacid,

H₂ receptor blocker, proton pump inhibitor)

- **Ileal resection, disease** (e.g. celiac disease)

Insufficient diet

- **Alcohol abuse**
- Chronic systemic disease, mental illness, advanced age
- Food insecurity
- Self-imposed dietary restrictions (e.g. **vegan**)

Adequate diet but increased requirements

- Pregnancy, lactation, malignancies
- Disease states with ↑ cellular turnover (e.g. chronic hemolysis, exfoliative skin disease)

Medication interfering with absorption

- E.g. Metformin, cycloserine, isoniazid, neomycin

Fish tapeworm *Diphyllobothrium latum* infestation

- Competes for absorption in ileum

Imerslund–Gräsbeck syndrome (juvenile megaloblastic anemia)

- Autosomal recessive disorder
- Vitamin B₁₂-intrinsic factor receptor defect

cbID inborn error of cobalamin metabolism

- MMADHC gene mutation → MMADHC protein defect (cobalamin transporter)

COMPLICATIONS

- **Macrocytic anemia**
- **Neurodegenerative disorder**

SIGNS & SYMPTOMS

- High body stores → 1–2 years insufficient intake → symptoms (adult/child)
- B₁₂-deficient mothers → infant cobalamin deficiency sequelae at age 6–18 months
- **Megaloblastic anemia**
 - Hypoxemia, tissue hypoxia → fatigue, activity intolerance, pallor, ↑ heart rate

- ↑ hemolysis → jaundice
- ↓ gastrointestinal tract mucosa integrity → atrophic glossitis, angular stomatitis, anorexia, nausea, diarrhea
- Impaired myelin production → cognitive impairment, paresthesias, impaired proprioception, gait disturbance, slowed cognition

DIAGNOSIS

LAB RESULTS

Blood study

- ↓ cobalamin
- CBC
 - ↓ RBC count; ↓ reticulocyte count; megaloblastic anemia (↑ MCV, ↓ MCH)
- Blood smear analysis
 - Macrocytosis, oval macrocytes; anisocytosis; poikilocytosis; **hypersegmented neutrophils**
- ↑ hemolysis markers
 - Elevated indirect bilirubin, lactate dehydrogenase, ↓ haptoglobin

Hypercellular bone marrow

TREATMENT

OTHER INTERVENTIONS

- ↑ dietary cobalamin
- Supplementation (cyanocobalamin)
 - Pernicious anemia → parenteral cobalamin
- Address complications

VITAMIN C DEFICIENCY

osms.it/vitamin-c-deficiency

PATHOLOGY & CAUSES

- Insufficient vitamin C for body's metabolic needs
- Body cannot synthesize, must obtain in diet
- **Active form:** L-ascorbic acid

RDA

- 9–13 years old: 45mg
- 14–18 years old: 75 mg (biologically-male); 65mg (biologically-female)
- 19+ years old: 90 mg (biologically-male); 75mg (biologically-female)
- **Pregnancy:** 85mg
- **Lactation:** 120mg
- **Smokers:** ↑ 35mg/day

RISK FACTORS

Insufficient diet

- Food insecurity
- Self-imposed dietary restrictions
- Chronic systemic disease, mental illness, advanced age
- Feeding infants evaporated/boiled cow's milk

↑ oxidative stress

- Smoking, secondhand smoke

COMPLICATIONS

- **Scurvy**, related sequelae (e.g. periodontal disease; bone, joint disorders)
- **Impaired wound healing**
- Weakened immune system
- Depression
- Microcytic **anemia**

SIGNS & SYMPTOMS

- ↓/no intake → symptoms within one month
- Mucocutaneous signs
 - Spongy gums → loose teeth
 - Capillary fragility → **petechiae**, **ecchymoses**, **perifollicular hemorrhage**, **subperiosteal hemorrhage**
 - Hair structure changes → **corkscrew hair**
- Inability to maintain bone matrix
 - Arthralgias, bone structure changes
- **Anemia**
 - Fatigue, malaise
- **Impaired wound healing**

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Sclerotic, lucent metaphyseal bands, soft tissue edema

TREATMENT

OTHER INTERVENTIONS

- ↑ dietary/supplementation vitamin C
 - Present in many **fruits**, **vegetables** (especially citrus, tomatoes, broccoli, bell peppers, potatoes)
 - Supplements, enriched grains
- Address complications



Figure 53.2 An X-ray of the leg of a child with scurvy. There is a dense zone of provisional calcification at the epiphysis, known as a Frankel line, with underlying radiolucency known as a Trümmerfeld zone.